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Epidemiological Analysis of Rare Polydactylies

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This work includes all cases with extra digits (polydactyly) registered from a birth sample of over four million births aggregated from two comparable birth series: the Latin-American Collaborative Study of Congenital Malformations: ECLAMC (3,128,957 live and still births from the 1967 to 1993 period), and the Spanish Collaborative Study of Congenital Malformations: ECEMC (1,093,865 livebirths from April 1976 to September 1993, and 7,271 stillbirths from January 1980 to September 1993).

All but 2 of 6,912 registered polydactyly cases fit well into one of the following 11 preestablished polydactyly types (observed number of cases in parentheses): Postaxial hexadactyly (5,345), Preaxial-I hexadactyly (1,018), Seven or more digits (57), synpolydactyly (15), crossed polydactyly (45), 1st digit triphalangism (33), 2nd digit duplication (39), 3rd digit duplication (18), 4th digit duplication (22), Haas polysyndactyly (3), and high degree of duplication (4).

The birth prevalence rates observed in both series were similar except for postaxial polydactyly, which was more frequent in the ECLAMC (150.2/100,000) than in the ECEMC (67.4/100,000), as expected due to the higher African Black ethnic extraction of the South-American than of the Spanish populations. This similar frequency for the rare polydactylies (5.4 per 100,000 in South America and 5.7 in Spain), and for each one of the 9 categories, suggests that the values reported here are valid for most populations.

The rare polydactylies are frequently syndromal: one third of them (77/236) were found in association with other congenital anomalies, 11.0% (26/236) in MCA cases and 21.6% (51/236) in recognized syndromes.

KEY WORDS: polydactyly, hexadactyly, synpolydactyly, polysyndactyly, triphalangism

INTRODUCTION

Extra digital rays are frequent anomalies in humans, and most of them include a duplication of the first (thumb/hallux) or fifth (finger/toe) digits, the remaining morphological types being rare [Castilla et al., 1973].

The classic genetic classification of Temtamy and McKusick [1978] of hand anomalies includes only those polydactylies inherited as Mendelian traits, while the more recently developed pathogenic classification of Winter and Tickle [1993] is too broad. The aim of this paper was not to develop a new classification of polydactylies but to describe the frequency and epidemiology of all existing polydactyly types. In order to do this, organization of the material into suitable classification was necessary.

MATERIALS AND METHODS

This study includes an unselected sample of all cases with polydactyly diagnosed in two consecutive and complete birth series: the Latin-American Collaborative Study of Congenital Malformations, ECLAMC [Castilla and Lopez-Camelo, 1990], and the Spanish Collaborative Study of Congenital Malformations, ECEMC [Martínez-Frías, 1994; Martínez-Frías and Urioste, 1994]. From 1967 to 1993, the ECLAMC surveyed a total population of 3,128,957 births (live and stillbirths), while the ECEMC surveyed 1,093,865 livebirths from April 1976 to September 1993, and 7,271 stillbirths from January 1980 to September 1993. The period 1980 to September 1993 is used to calculate the prevalence figures in the ECEMC data, while the total cases (live and still births) with rare polydactylies are considered for the study of the descriptive characteris-

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tics. Both programs are hospital-based, case-control studies, and surveillance systems, and in both of them the next non-malformed baby of the same sex born in the same hospital is selected as a control subject for each case. ECLAMC and ECEMC are clinically oriented studies, rather than epidemiologic systems, having very similar methodology and working definitions, ensuring comparable results.

The polydactylies were described according to standardized pre-established descriptive norms including: affected limbs, duplicated digits, and, for the extra digits, level of implantation (carpal/tarsal, metacarpal/metatarsal, proximal, middle or, distal phalanx) number of phalanges, type of base (sessile or pedunculated), and presence of nail or not.

This work focuses on the rare polydactyly types, defined as other than hexadactyly due to first or fifth digit duplications, that is, excluding postaxial (A and B), and preaxial-1 types of Temtamy and McKusick [1978], which are only shown in Table I just to illustrate the comparability of the two birth series presented here.

Polydactyly cases were subdivided into "multiple" and "single" if other unrelated birth defect was or was not observed in the same infant. The latter group included "isolated" and "combined" cases, when no other defect was described, and when an interrelated limb defect was present in the same infant, respectively. The "combined" subgroup included mainly syndactylies taken as pathogenetically related to polydactyly [Castilla et al., 1977]. The "multiple" group included known "syndromes" and cases with MCA (multiple congenital anomaly) patterns.

All rare polydactyly cases fitted into one, and only one, of the following nine categories:

1) Seven or more digits. More than six digits in at least one limb. It corresponds with preaxial-4 [Temtamy and McKusick, 1978], or pre+post-axial [Winter and Tickle, 1993].

2) Synpolydactyly. Syndactyly between 3rd and 4th fingers, and/or between 4th and 5th toes, with an extra digit into the web, MIM 18600 [McKusick, 1994]. It also corresponds to mesoaxial polydactyly [Winter, Tickle and 1993].

3) Crossed polydactyly. Preaxial polydactyly in one limb and postaxial in another. Cases with both polydactyly types in the same limb were placed into the Seven or more digits category.

4) 1st digit triphalangism. Thumb (opposable or not), or hallux, with three phalanges. It corresponds to preaxial-2 [Temtamy and McKusick, 1978].

5) 2nd digit duplication. One case with duplications of 2nd left finger and 3rd left toe was included here. It corresponds to preaxial-3 [Temtamy and McKusick, 1978].

6) 3rd digit duplication. One case with duplications of 3rd right finger and both 1st toes was included here. As with the case mentioned above, included as a 2nd digit duplication, the hand polydactyly was used for classification.

7) 4th digit duplication. Duplication of 4th finger or toe.

8) Haas poly-syndactyly: Complete syndactyly of all digits, except the first, plus one or more extra digits, affecting at least one limb, MIM 186200 [McKusick, 1994]. It corresponds to abnormal patterning [Winter and Tickle, 1993].

9) High degree of duplication: Mirror image partial or complete duplication of hand and/or foot. Cases with 7 or more digits are included here as long as they present a mirror pattern.

TABLE I. Polydactyly Birth Prevalence Rates (/100,000) in South America (ECLAMC), and in Spain (ECEMC)*

		ECLAMC		ECEMC[a]	
Polydactylies		Number	Rate	Number	Rate
Period		1967–1993		1980–1993	
Births		3,128,957	—.–	957,157	—.–
Postaxial:	Single	4,160	132.9	486	50.8
	Multiple	540	17.3	159	16.6
	Total	4,700	150.2	645	67.4
Preaxial-I:	Single	628	20.1	180	18.8
	Multiple	149	4.7	61	6.4
	Total	777	24.8	241	25.2
Rare:	Single	123	3.9	29	3.0
	Multiple	46	1.5	26	2.7
	Total	169	5.4	55	5.7
Unspecified:	Single	136	4.4	23	2.4
	Multiple	139	4.4	26	2.7
	Total	275	8.8	49	5.1
Total:	Single	5,042	161.1	718	75.0
	Multiple	880	28.1	272	28.4
		(14.9)		(27.5)	
	Total	5,922	189.3	990	103.4

* ( ), % of multiples.
[a] Data for calculation of the prevalence rates in ECEMC correspond to the period 1980–1993, including live and still births.

TABLE II. Polydactyly Birth Prevalence Rates (/100,000) for Nine Categories of Rare Polydactylies

	ECLAMC		ECEMC[a]		Total	
Rare polydactylies	N	Rate	N	Rate	N	Rate
Seven or more digits	35	1.1	19	2.0	54	1.3
Synpolydactyly	14	0.5	1	0.1	15	0.4
Crossed polydactyly	35	1.1	8	0.8	43	1.1
1st digit triphalangism	21	0.7	8	0.8	29	0.7
2nd digit duplication	31[b]	1.0	8	0.8	39	1.0
3rd digit duplication	16	0.5	2[c]	0.2	18	0.4
4th digit duplication	12	0.4	7	0.7	19	0.5
Haas polysyndactyly	3	0.1	0	0.0	3	0.1
High degree of duplication	2	0.1	2	0.2	4	0.1
Total	169	5.4	55	5.7	224	5.5

[a]ECEMC figures correspond to the period 1980–1993.
[b]Includes one case with duplications of 2nd left finger and 3rd left toe.
[c]Includes one case with duplications of 3rd right finger and both 1st toes.

RESULTS

Frequencies

Table I shows the birth prevalence of all types of polydactylies in the two studied populations: South-America-ECLAMC and Spain-ECEMC. Only about 5% of polydactyly cases had incomplete description not allowing their classification (324/6,912 = 4.69%). The overall frequency of all types of polydactylies is higher in South-America than in Spain (189.3 and 103.4 per 100,000, respectively). The difference between the two populations is largely based on the statistically significant ($P < 0.01$) higher rates of the single postaxial type (5th digit duplication) in the ECLAMC (132.9 per 100,000) than in the ECEMC (50.8 per 100,000). The rates of the different clinical presentations of preaxial-I polydactyly are similar in both populations. Table I also shows that for rare polydactylies, the proportion of cases with other unrelated congenital defects is significantly higher ($P < 0.006$) in the ECEMC data (26/55 = 47.3%) than in the ECLAMC (46/169 = 27.2%), probably due to differences in the inclusion of minor/mild anomalies in each program.

Table II shows that after exclusion of the two common polydactyly types: Preaxial-I (duplication of the first digit), and postaxial (duplication of the fifth digit), the cases with rare polydactylies are distributed into the above mentioned nine categories. This Table II indicates the birth prevalence of each category by study population. The birth prevalence rates of each category varies between 1.3 per 100,000 and 1 per 1,000,000, while the overall frequency of all together is 5.5 per 100,000, showing no significant differences between the ECLAMC and ECEMC prevalence figures.

Table III depicts the 236 cases with rare polydactylies, including all cases live and stillborn from the ECEMC program, by clinical presentation. Although there are some slight differences, most of the different groups of rare polydactylies are more frequently observed as a single malformation.

Demographic and Familial Data

Tables IV and V depict the demographic and family data for each rare polydactyly type of the ECLAMC (Table IV) and ECEMC (Table V), together with the

TABLE III. Distribution of Rare Polydactyly Cases by Clinical Presentation*

	ECLAMC				ECEMC[a]				Total			
Rare polydactylies	Sin	MCA	Syn	Total	Sin	MCA	Syn	Total	Sin	MCA	Syn	Total
Seven or more digits	20	1	14	35	6	8	8	22	26	9	22	57
Synpolydactyly	14	0	0	14	1	0	0	1	15	0	0	15
Crossed polydactyly	23	2	10	35	9	1	0	10	32	3	10	45
1st digit triphalangism	15	4	2	21	7	3	2	12	22	7	4	33
2nd digit duplication	27[b]	1	3	31	7	0	1	8	34	1	4	39
3rd digit duplication	10	3	3	16	1	1[c]	0	2	11	4	3	18
4th digit duplication	11	1	0	12	8	1	1	10	19	2	1	22
Haas polysyndactyly	0	0	3	3	0	0	0	0	0	0	3	3
High degree of duplication	2	0	0	2	0	0	2	2	2	0	2	4
Total	122	12	35	169	39	14	14	67	161	26	49	236

* Sin, single; MCA, multiple congenital anomalies; Syn, syndromes.
[a] ECEMC data correspond to live and still born cases during the period 1976–1993.
[b] Includes one case with duplications of 2nd left finger and 3rd left toe.
[c] Includes one case with duplications of 3rd right finger and both 1st toes.

TABLE IV. Demographic Data for the ECLAMC Birth Series, and Single Rare Polydactyly Cases in Eight of Nine Categories (No single cases of Haas polysyndactyly)*

			Cases							
		Births	7+	Synp	Cros	Tri	2nd	3rd	4th	HDD
Examined infants	N	3128957	20	14	23	15	27	10	11	2
Sex										
Male	N	1598460	11	7	15	2	21	6	4	1
Female	N	1524391	9	7	8	13	6	4	7	1
M/F Index		1.05								
Twins										
Yes	N	405 (0.9)	0	0	0	1	1	0	1	0
No	N	43990	20	14	23	14	26	10	10	2
Perinatal death										
Yes	N	727 (1.7)	1	0	0	0	1	0	0	0
No	N	42925	19	13	21	15	25	10	11	2
Birth weight										
	N	44230	20	14	22	15	27	10	11	2
	Mean	3197.1	3222.0	3337.1	3247.7	2814.3	3104.4	3074.0	3362.7	[a]
	SD	567.8	615.0	454.9	774.4	907.5	789.1	660.7	510.8	
Gestational age										
	N	38545	6	12	14	7	14	4	3	2
	Mean	38.9	39.3	39.8	38.8	37.9	37.7	39.5	38.0	[b]
	SD	2.6	1.2	1.6	3.8	4.1	3.1	1.9	1.0	
Maternal age										
	N	44283	19	14	23	15	27	10	11	2
	Mean	25.3	23.4	26.4	23.6	22.1	25.4	23.0	29.4	[c]
	SD	6.3	6.5	5.3	5.1	5.6	7.0	5.3	7.7	
Parity										
1	N	14829 (33.5)	9	4	9	7	11	5	3	0
2+	N	29501	10	10	14	8	15	5	8	2
Paternal age										
	N	41172	8	13	14	8	14	4	3	2
	Mean	29.1	30.0	30.8	29.9	26.5	30.8	27.8	33.0	[d]
	SD	7.4	8.2	7.4	8.1	7.9	7.3	6.6	11.1	
Consanguinity										
Yes	N	435 (1.1)	0	0	0	0	0	0	0	1
No	N	40993	8	13	14	7	14	4	3	1
Family history										
Yes	N	362 (0.9)	3	4	5	2	3	0	3	1
No	N	41653	5	9	9	6	11	4	0	1
Ethnicity										
Lat-Europ	N	2550 (6.4)	0	1	1	0	1	0	0	0
Mestizo	N	27292 (68.5)	6	9	10	5	7	3	2	2
Blacks	N	6574 (16.5)	0	0	2	2	4	0	1	0
Other	N	3466 (8.7)	2	2	1	0	2	1	0	0
Total	N	39882 (100)	8	12	14	7	14	4	3	2

* ( ), percentages. 7+, Seven or more digits; Synp, Synpolydactyly; Cros, Crossed polydactyly; Tri, 1st digit triphalangism; 2nd, 2nd digit duplication; 3rd, digit duplication; 4th, digit duplication; HDD, High degree of duplication.
[a] 2,600 and 2,630 g.
[b] 38 and unknown weeks.
[c] 17 and 22 years.
[d] 27 and 48 years.

information from the population in which cases were ascertained. Only single cases are included in this analysis.

A family history of polydactyly of any type (21/66 = 31.8% in the ECLAMC, and 14/39 = 35.9% in the ECEMC) was more frequently observed than in the general population (0.9% in the ECLAMC, and 0.3% in the ECEMC). Thus, the expected number of cases in each program are 0.6 and 0.12, respectively, the differences with the observed numbers (21 and 14) being statistically significant ($Z=26.3$, $P < 0.01$ in the ECLAMC, and $Z=40.1$, $P < .01$ in the ECEMC).

Cases do not depart from expected values for sex, twinning, perinatal mortality, birth weight, gestational age, parental ages, parity, parental consanguinity, or ethnicity. Even when the small observed numbers do not permit statistical analysis, data are presented to allow further utilization. However, considering both series together (Tables IV and V) and even without reaching statistical significance, triphalangism of the first digit had frequent twinning (3/20 total cases), as well as low birth weight (ECLAMC: 2,814 ± 907.5 g; ECEMC 2,761 ± 702.0 g), and low gestational age (ECLAMC 37.9 ± 4.1 weeks; ECEMC 39 ± 2.4 weeks). Furthermore, this polydactyly type presented a very low sex ratio in the ECLAMC material (2 males and 13 females observed, 7.67 and 7.32 expected; X^2:8.60; df:1; $P < 0.01$), but not in the ECEMC

TABLE V. Demographic Data for the ECEMC Birth Series, and Single Rare Polydactyly Cases in Seven of Nine Categories (No single cases of Haas polysyndactyly and High Degree of Duplication)*

			Cases						
		Births	7+	Synp	Cros	Tri	2nd	3rd	4th
Examined infants	N	1093065	6	1	9	7	7	1	8
Sex									
Male	N	562930	6	1	3	6	5	0	4
Female	N	530830	0	0	6	1	2	1	4
M/F Index		1.06							
Twins									
Yes	N	165 (0.8)	0	0	0	2	0	0	0
No	N	20530	6	1	9	5	7	1	8
Perinatal death									
Yes	N	32 (0.15)	0	0	0	0	0	0	0
No	N	20616	6	1	8	7	7	1	8
Birth weight									
	N	20729	6	1	9	7	7	1	8
	Mean	3316.5	3625.0	3170	3257.2	2761.4	3232.1	2900	3328.8
	SD	476.3	823.6		796.4	702.0	466.2		720.4
Gestational age									
	N	19601	5	1	9	7	7	1	7
	Mean	39.5	39.4	40	39.3	39.0	38.7	34	40.6
	SD	1.8	1.1		2.4	2.4	1.5		1.7
Maternal age									
	N	20750	6	1	9	7	7	1	8
	Mean	27.3	27.8	24	27.8	25.4	29.9	31	30.3
	SD	5.4	5.1		4.7	1.8	7.1		6.8
Gestation									
1	N	8484 (40.9)	1	0	4	6	1	1	4
2+	N	12264	5	1	5	1	6	0	4
Paternal age									
	N	20304	6	1	9	7	7	1	8
	Mean	30.2	30.8	27	30.6	28.4	33.3	31	32.3
	SD	5.8	4.0		5.3	3.3	5.4		7.6
Consanguinity									
Yes	N	402 (2.0)	1	0	1	0	0	0	0
No	N	19900	5	1	8	7	7	1	8
Family history									
Yes	N	52 (0.3)	2	0	7	3	1	0	1
No	N	18509	4	1	2	4	6	1	7
Ethnicity									
Lat-Europ	N	17751 (97.9)	4	1	9	7	7	1	8
Mestizo	N	50 (0.3)	0	0	0	0	0	0	0
Blacks	N	28 (0.2)	0	0	0	0	0	0	0
Gipsies	N	297 (1.5)	0	0	0	0	0	0	0
Other	N	8 (0.1)	0	0	0	0	0	0	0
Total	N	18134 (100)	4	1	9	7	7	1	8

* ( ), percentages. 7+, Seven or more digits; Synp, Synpolydactyly; Cros, Crossed polydactyly; Tri, 1st digit triphalangism; 2nd, 2nd digit duplication; 3rd, digit duplication; 4th, digit duplication; HDD, High degree of duplication.

data (6 males and 1 female observed, 3.60 and 3.40 expected; X^2:3.29; df:1; $P > .05$).

Morphological Characteristics

Table VI presents the morphological characteristics of the rare polydactylies and their association with other pathogenetically unrelated defects in the same infant.

1) Seven or more digits. The 57 cases, with similarly affected hands or feet, about half of them (N 31) were bilateral, and also half were multiple (N 31) (MCA and syndromal).

2) Synpolydactyly. Feet were more frequently affected (N 11) than hands (N 5) among the 15 cases observed, all of them being single, with no other unrelated anomalies. None of the 15 cases had other associated anomalies.

3) Crossed polydactyly. The most frequent subtype was duplications of fifth finger and first toe (35/45 cases), while duplication of first finger and fifth toe was next in frequency, with only 6 cases. Most cases (32/45) had no other anomalies.

4) 1st digit triphalangism. Thumbs (30/33 cases) were more frequently affected than hallux (3/33), one case having both, thumbs and hallux involved, and most cases (20/33) were single-isolated.

5) 2nd digit duplication. Duplication of the second toe (25/39) was more frequent than that of the second finger (15/39). Only 4/39 cases had isolated bilateral du-

TABLE VI. Rare Polydactylies: Number of Cases According to Concurrent Anomalies and Affected Limbs (Both series pooled)*

				Hand		Foot		Both		
				Un	Bi	Un	Bi	Un	Bi	Total
Seven or more digits:	Single:	Isolated		5	2	3	4	0	0	14
		Combined		2	1[a]	4	3	0	2	12
	Multiple:	MCA		4	0	4	0	0	1	9
		Syndromes		5	6	3	3	1	4	22
Synpolydactyly:	Single:	Isolated		2	0	9	1	0	1	13
		Combined		0	2	0	0	0	0	2
	Multiple:	MCA		0	0	0	0	0	0	0
		Syndromes		0	0	0	0	0	0	0
Crossed polydactylies:	Single:	Isolated	HI/HV	0	0	0	0	0	1	1
			FI/FV	0	0	0	1	0	0	1
			HI/FV	0	0	0	0	0	0	0
			HV/FI	0	0	0	0	2	6	8
			HV/FI-V	0	0	0	0	0	2	2
		Combined	HI/HV	0	0	0	0	0	0	0
			FI/FV	0	0	0	0	0	0	0
			HI/FV	0	0	0	0	0	0	0
			HV/FI	0	0	0	0	2	17[b]	19
			HV/FI-V	0	0	0	0	0	1	1
	Multiple:	MCA	HI/HV	0	0	0	0	0	0	0
			FI/FV	0	0	0	0	0	0	0
			HI/FV	0	0	0	0	0	1	1
			HV/FI	0	0	0	0	1	1	2
			HV/FI-V	0	0	0	0	0	0	0
		Syndromes	HI/HV	0	0	0	0	0	0	0
			FI/FV	0	0	0	0	0	0	0
			HI/FV	0	0	0	0	0	3	3
			HV/FI	0	0	0	0	0	6	6
			HV/FI-V	0	0	0	0	0	1	1
Triphalangeal 1st digit:	Single:	Isolated		7	11	0	0	1	1	20
		Combined		2	0	0	0	0	0	2
	Multiple:	MCA		4	2	0	1	0	0	7
		Syndromes		3	0	0	0	1	0	4
Duplicated 2nd digit:	Single:	Isolated		2	4	18	1	0	0	25
		Combined		5	0	3	0	1[c]	0	9
	Multiple:	MCA		0	1	0	0	0	0	1
		Syndromes		1	1	2	0	0	0	4
Duplicated 3rd digit:	Single:	Isolated		2	1	4	0	0	0	7
		Combined		2	0	1	1	0	0	4
	Multiple:	MCA		1	0	2	0	0	1[d]	4
		Syndromes		0	0	2	1	0	0	3
Duplicated 4th digit:	Single:	Isolated		7	1	8	1	0	0	17
		Combined		2	0	0	0	0	0	2
	Multiple:	MCA		0	0	1	1	0	0	2
		Syndromes		0	0	0	1	0	0	1
Haas polysyndactyly:	Single:	Isolated		0	0	0	0	0	0	0
		Combined		0	0	0	0	0	0	0
	Multiple:	MCA		0	0	0	0	0	0	0
		Syndromes		0	0	0	0	0	3	3
High degree of duplication:										
	Single:	Isolated		0	0	0	1	0	0	1
		Combined		0	0	1	0	0	0	1
	Multiple:	MCA		0	0	0	0	0	0	0
		Syndromes		0	0	0	2	0	0	2

* Un, Unilateral; Bi,Bilateral.
[a] Includes one case with AD polysyndactyly.
[b] Includes two cases with AD polysyndactyly.
[c] Includes one case with duplications of 2nd left finger and 3rd left toe.
[d] Includes one case with duplications of 3rd right finger and both 1st toes.

plication of the index finger, so fitting into the description of preaxial-3 polydactyly.

6) 3rd digit duplication. Most cases were single (11/18), and feet (12/18 cases) were more frequently affected than hands (7/18 cases).

7) 4th digit duplication. Most cases were single (19/22), and hands (10/22 cases) and feet (12/22 cases) were equally affected.

8) Haas poly-syndactyly. Haas polysyndactyly excluded cases with Haas syndactyly, namely, complete

finger or toe syndactyly without duplicated digits. Three cases were observed, all 3 from ECLAMC, all of them tetramelic.

9) High degree of duplication: In all four cases only feet were affected, both in three of them. Two cases were single and two were syndromic.

Associated Defects

Combination with other limb anomalies, mainly syndactylies, was observed in 22.0% of cases (52/236), and this was most common among the crossed polydactylies (20 of 45 cases), and the 7 or more digits (12 of 57 cases) (Table VI).

The 26 cases of rare polydactylies considered as nonclassified MCA infants will be published elsewhere in a work dedicated to the association of polydactylies, rare or not, with other congenital anomalies.

Table VII presents the distribution of the different observed syndromes in the nine study categories of rare polydactylies. Among the total of 50 cases with syndromes and rare polydactylies, 11 (22%) were chromosomal, 38 (76%) had different genetic conditions, and 1 (2%) was clue to an thalidomide embryopathy.

A known syndrome was identified in 50 of the 74 cases with a rare polydactyly and other unrelated defects. Seven cases had a short rib-polydactyly syndrome, including two Majewski, one Saldino-Noonan, and four undefined sub-types, six of them being of the 7 or more digits category (Table VII).

With six cases each, rare polydactylies were observed in Mohr oro-facio-digital syndrome type II (five of them with seven or more digits), and Meckel syndrome (with no consistent subtype). Varadi oro-facio-digital syndrome type VI was seen in three cases, two with crossed and one with seven digits or more. With two cases each, the following syndromes were registered: Ellis-van Creveld, Rubinstein-Taybi, oro-facio-digital I, Aase, and Apert. Carpenter, hydrolethalus, thalidomide embryopathy, Hoyme, acrocallosal, Laurin-Sandrow, and Bartsocas-Papas syndromes were observed in one case each.

Among the chromosome anomalies, trisomy 13 was seen in six cases, comprising three different types of polydactyly, Down syndrome in three cases, trisomy 18, and an undefined chromosome anomaly in one case each. This last case had a 47,XY,+E karyotype, with an unspecified extra chromosome.

DISCUSSION

We have analyzed a large population of more than 4,000,000 births from two different programs in order to determine the birth prevalence of different types of polydactyly. We have also described the characteristics of the rare types of polydactyly that were those different from preaxial (first digit duplication) and postaxial (fifth digit duplication) polydactylies. It is interesting that the only significant difference between the prevalence of each type of polydactyly observed between South America and Spain is in relation to the prevalence of the postaxial type. The larger proportion of Black African ancestry in the South-American population could explain this result [Castilla et al., 1973]. Another difference between both series was the higher proportion of infants with MCA patterns observed in the ECEMC than in the ECLAMC, which could be due to differences in the inclusion of minor/mild defects between both programs.

With the only exception of the two cases indicated in footnotes [b] and [c] in Table II, the nine anatomical categories sufficed to fit all cases with rare polydactylies.

TABLE VII. Multiple Rare Polydactylies*

	7+	Synp	Cros	Tri	2nd	3rd	4th	Haa	HDD	Total
13 trisomy	2	0	2	0	0	1	1	0	0	6
18 trisomy	0	0	0	0	0	1	0	0	0	1
Down	0	0	0	1	2	0	0	0	0	3
Chromosome anomaly	0	0	0	0	1	0	0	0	0	1
SRP Majewski	1	0	1	0	0	0	0	0	0	2
SRP Saldino-Noonan	1	0	0	0	0	0	0	0	0	1
SRP NFS	4	0	0	0	0	0	0	0	0	4
Ellis-van Creveld	2	0	0	0	0	0	0	0	0	2
Rubinstein-Taybi	1	0	1	0	0	0	0	0	0	2
OFD-I	2	0	0	0	0	0	0	0	0	2
OFD-II/Mohr	5	0	1	0	0	0	0	0	0	6
OFD-VI/Váradi	1	0	2	0	0	0	0	0	0	3
Meckel	3	0	1	0	1	1	0	0	0	6
Carpenter	0	0	1	0	0	0	0	0	0	1
Hydrolethalus	0	0	1	0	0	0	0	0	0	1
Thalidomide	0	0	0	1	0	0	0	0	0	1
Aase	0	0	0	1	0	0	0	0	0	1
Hoyme	0	0	0	1	0	0	0	0	0	1
Acrocallosal	0	0	0	0	0	0	0	0	1	1
Laurin-Sandrow	0	0	0	0	0	0	0	0	1	1
Apert	0	0	0	0	0	0	0	2	0	2
Bartsocas-Papas	0	0	0	0	0	0	0	1	0	1
Total	22	0	10	4	4	3	1	3	2	49

* Number of cases according to syndromes involved; Nine categories: 7+, Seven or more digits; Synp, Synpolydactyly; Cros, Crossed polydactyly; Tri, 1st digit triphalangism; 2nd, 2nd digit duplication; 3rd, 3rd digit duplication; 4th, 4th digit duplication; Haa, Haas polysyndactyly; HDD, High degree of duplication.

Since the cases derive from >4,000,000 births, it is quite likely that this classification system also fits all cases from other studies.

Although syndrome identification is not the aim of this analysis, it seems evident that the rare polydactylies are frequent in syndromes. In spite of the difficulty in syndrome diagnosis at birth, 12 of the 43 different syndromes presented by Winter et al. [1988] with polydactyly were recognized in one or more cases in this material.

The characteristics of each category of rare polydactyly may be summarized as follows:

1) Seven or more digits (heptadactyly and higher): This category could include some cases of polysyndactyly or preaxial polydactyly-IV, MIM 174700 [McKusick, 1994]. It is frequently observed in infants with other anomalies whether in syndromes or in infants with MCAs, while the isolated cases usually show a family history compatible with autosomal dominant inheritance.

2) Synpolydactyly: This well-known autosomal dominant anomaly, MIM 18600 [McKusick, 1994], was registered with a higher frequency in the South-American than in the Spanish birth series, suggesting ethnic differences. As reported by other authors, most cases had affected feet [Sayli et al., 1995]. Homozygous cases as described by Akarsu et al. [1995] were not observed.

3) Crossed polydactyly: This anomaly is MIM 174700 [McKusick, 1994], including type-1 (duplicated fifth finger and hallux), as well as type-2 (duplicated thumb and fifth toe) crossed polydactyly, among others [Ishikirimaya et al 1991]. In 10 cases a syndrome was recognized, none of them being Greig syndrome, probably overlooked at birth due to its mild facial anomalies [Baraitser et al 1983].

4) 1st digit triphalangism: This is a heterogeneous group of anomalies, MIM 174500 [McKusick, 1994], probably underascertained at birth since is less conspicuous that all other polydactyly types due to its normal number of digital rays. The thalidomide embryopathy baby was born in 1991 to a mother being treated for leprosy, a preposterous situation that still exists in South America [Rocha, 1994]. The female excess observed only in the ECLAMC data could be another expression of the causal heterogeneity of this polydactyly type.

5) 2nd digit duplication: Even when this category includes the autosomal dominant preaxial-III polydactyly, MIM#174600 [McKusick, 1994], most cases seem not to belong to this rare mutation. Unfortunately, the present material does not have the radiological information for the metacarpal epiphysis of the extra digit, said to be consistently distal in preaxial-III polydactyly [Swanson and Brown, 1962].

6) 3rd digit duplication: Eighteen cases were registered into this rare anomaly for which no reference could be found in the literature. None of the 12 single cases were familial, and no consistent pattern of association with other anomalies were seen among the 3 MCAs and 3 syndromic cases.

7) 4th digit duplication: This very rare polydactyly was seen as the only congenital anomaly in almost all cases, and it was frequently familial.

8) Haas polysyndactyly: This anomaly is almost exclusive of Apert acrocephalo-polysyndactyly which is the diagnosis for two of the three registered cases. However, a third case had this type of polysyndactyly associated with other anomalies fitting into a diagnosis of Bartsocas-Papas syndrome, which is rather unexpected.

9) High degree of duplication: This easily recognized anomaly was correlated with the mutant disorganization in the mouse [Hummel, 1959; Winter and Donnai, 1989]. In two cases the anomaly was part of a syndrome, one in an acrocallosal, and the other has been published as a Laurin-Sandrow syndrome [Martínez-Frías et al., 1994].

In conclusion, this is the first time the population frequency of the different types of polydactylies are analyzed simultaneously in a large population of births. Since South America and Spain present almost identical overall frequencies for the rare polydactylies (5.4 per 100,000 in South America and 5.7 in Spain), and for each one of the nine categories, it is likely that the frequency values observed here are valid for most populations.

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